site PuPuPuC(A/T). The way in which the DNA-binding dimer observed in the crystal relates to the tetramer is not clear, although a model has been constructed¹. A third question revolves around the incredibly diverse set of p53 mutations found in tumours. Although the most common mutations can be explained as described above, there are many rare mutations that also seem to inactivate the protein and are distributed over 125 different amino acids within the core domain. Nothing in the X-ray structure unambiguously reveals why so many residues in p53 can have such a drastic effect on function, or why (and indeed, whether) p53 amino acids are more functionally interconnected' than those in other DNA-binding proteins.

Cho and colleagues conclude their article with the statement that the crystal structure "solidifies the hypothesis that DNA binding and transactivation are the critical activities required for tumour suppression". The beauty and simplicity of this hypothesis, however, is challenged by the paper from Caelles et al.2. The normal p53 gene suppresses tumour growth by causing cells to arrest in the G1 phase of the cell cycle or by causing them to become so disgruntled with their physiological state that they commit suicide (apoptosis)¹⁰. Caelles *et al.* immortalized pituitary cells with the simian virus SV40 T-antigen and then transferred a temperature-sensitive p53 gene into the cells. Following irradiation, the cells became apoptotic only when the wild-type p53 gene product was expressed at the permissive temperature. What was novel about this p53-dependent apoptosis was that it was not inhibited by hefty doses of transcription or translation inhibitors. Of course, it is impossible to exclude the possibility that some genes escaped the inhibition. In this regard, it would be interesting to examine the p53-dependent expression of Bax, a Bcl-2-binding and apoptosis-inducing gene product11 However, the most straightforward interpretation of the data is that p53-induced apoptosis in this system was not brought about by the sequence-specific transactivation of genes, but was the result of some other functional property of p53 (ref. 2).

How do these results compare with others? One of the most important of the systems relating p53 to apoptosis involves p53 'knockout' mice^{12,13}. Thymocytes from these mice are resistant to apoptosis upon X-irradiation, unlike those of normal mice. Transcription and translation inhibitors block p53-dependent apoptosis in thymocytes¹⁴, unlike the situation in the pituitary cells. It is possible, as suggested by Caelles et al., that some of the effects of p53 (for example, G1 arrest) may be related to sequence-specific transactivation while others (apoptosis, at least in certain contexts) may be dependent on other actions of p53. Perhaps the unusual structure of p53 is telling us that p53 does something important besides activating expression of target genes. The results of Caelles et al. should provoke a careful re-examination of the necessity for transcription and translation in p53-mediated phenomena, and a renewed search for the

critical biochemical properties of p53 in situations where specific gene activation is not involved.

Whatever the normal function(s) of p53 in growth control, it is clear that the mutants have lost them (or they would not have been selected for in vivo). One practical goal of p53 research is therefore to convert mutant p53 proteins to wildtype forms. The structure of p53 provides an entirely new and powerful step towards this goal¹. Can small molecules be found. for example, that link the L and LH loops of p53 in proteins containing an Arg 175 mutation? How about a drug that allows a mutant of Arg 273 to bind to the phosphate that the wild-type amino acid normally contacts? The design of such 'restoring' compounds is no mean feat. but it is likely that computer modelling programs in both industry and academia will soon be humming the same X-raystimulated tune.

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CLIMATE -

Maize suffers a sea-change

Cynthia Rosenzweig

THE paper by Cane, Eshel and Buckland¹ on page 204 of this issue marks a seachange in climate forecasting on a global scale. Indices of sea surface temperatures in the eastern equatorial Pacific Ocean are, they find, remarkably highly correlated with maize yields in Zimbabwe, on the other side of the world. Intriguingly, these correlations exceed those between the same indices and annual precipitation. The forecasts can be made far enough in advance to be useful in agricultural management. Foreknowledge of drought - in advance of sowing — allows farmers to plant more drought-tolerant crop varieties or species. Predictions of the El Niño cycle and their practical consequences are thus joined, with strong statistical significance.

El Niño/Southern Oscillation (ENSO) events, which tend to recur every two to nine years, are related oceanic and atmospheric phenomena, characterized by increases in sea surface temperatures of the tropical Pacific Ocean, suppression of upwelling nutrient-rich water along the coast of South America and disruption of the trade winds. The cycle has long been known to be a large component of natural interannual climate variability in the tropics and subtropics, and to a lesser

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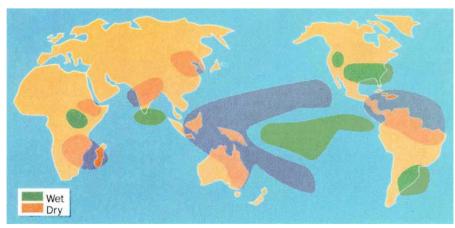


FIG. 1 World map showing the areas affected by El Niño (source: N. Nicholls in ref. 4).

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extent, in the mid-latitude regions. Global 'teleconnections' (relationships between weather at two or more distant points) linked to ENSO include lower-thannormal precipitation in western Oceania, India, southeastern Africa and northeastern South America, and excessive precipitation in western South America and eastern equatorial Africa² (see Fig. 1). In 1991–93, the last El Niño event (which was of moderate intensity) corresponded with an extremely severe drought in southeastern Africa.

After years of basic research to improve understanding of El Niño mechanisms that has culminated predictive models³, atmospheric scientists are now collaborating with social scientists to lay the foundations for applied research. In this case, Cane, a leading ENSO modeller, has worked with Buckland, an agricultural economist of the Southern Africa Development Community's Food Security Technical and Administrative Unit, to study the predictability of climate impacts on maize production. The potential for warning farmers in advance of drought and allowing them to prepare for it not only in Zimbabwe, but in other regions of the world - brings science, literally, right down to ground level.

Such strong climate perturbations have also long been known to have considerable effects on human activities. Indeed, it was the collapse of the anchovy fisheries off the western

shore of South America that first brought the El Niño cycle to widespread public awareness in 1972–73. ENSO events, particularly the extreme weather patterns of 1982–83, have been associated with damage to coastal resources, agriculture, transportation, housing and human life in five continents.

Crop productivity (both the quantity and quality of the output) in any location depends on a complex combination of climate, biophysical factors and management. The present study considers only one local climate variable, total annual precipitation. Although this is clearly correlated with crop yield, variations in the frequency, intensity and duration of rainfall all affect a standing crop differently. Deeper understanding of ENSO-driven effects on crop growth, and solving the riddle of why ENSO is more highly correlated with crop yield than with precipitation in Zimbabwe, will depend on

the inclusion of a wider range of variables and timescales. How ENSO affects agriculture also depends on how the biophysical field-level effects (including those on pests) lead to socioeconomic changes. Decisions made by farmers in the face of climate variability ultimately involve the success or failure of individual farms and, by extension, of entire regions, even of national economies highly dependent on agricultural products.

So far, work on ENSO-related impacts,

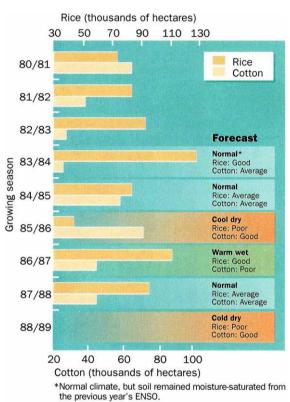


FIG. 2 Agricultural area sown to rice and cotton in the northern coastal region of Peru. ENSO forecasts began before the 1983–84 growing season (source: ref. 5).

including this study by Cane *et al.*, has been done primarily on a country-by-country basis⁴. Although such studies are rich in regional detail, their weakness is that they lack a common context; results can easily become anecdotal. A firmer framework is required, so that knowledge gained in one location (for example, what works and what does not) can be compared and applied in others. The climatological, agronomic and economic datasets and models already available should be marshalled to address the ENSO phenomenon, enabling valuable case studies to be embedded in a larger context.

Predictive activities are already under way in some countries. In Peru, ENSO forecasts are incorporated into national planning for the agricultural sector, and areas planted with rice and cotton (cotton being the more drought-tolerant crop) are adjusted accordingly, as Fig. 2 shows⁵. Governmental and intergovernmental

institutions, including the Inter-American Institute for Global Change Research and the US National Ocean and Atmospheric Agency, are fostering nascent programmes to aid the effective use of ENSO forecasts.

Economists have an important role to play in determining the economic value of climate forecasts. The expected 'value' represents the sum of the net gains to individual countries and groups of an optimal response to the forecasts, as compared with the alternative of 'business-asusual'. These gains must be weighted by the *ex ante* probabilities of various possible weather and climate conditions. The value of knowledge of the climate system includes not only better agricultural performance, but other benefits such as avoidance of flood damage and improved nutrition and health.

As ENSO climate forecasting grows out of the research mode into operational mode, awareness of and sensitivity to the costs of prediction errors also grows. Although simple correlations between El Niño events and maize yields in Zimbabwe are suggestive, more sophisticated testing is needed. Honesty about the limitations of any forecast is essential, especially when human livelihood is at stake.

What of the immediate future? Zebiak and Cane's current ENSO forecast based on their model⁶ indicates that equatorial Pacific sea surface temperatures will be slightly above normal during November to March (the next growing season in Zimbabwe), but enough to be considered a warm event. This is roughly the consensus of other long-range forecasts, which range from slightly below to somewhat above the mean. The implication is that maize yields in Zimbabwe will be normal or slightly below normal next year. A note of caution: over the past few months the forecasts have tended towards warmer temperatures. Zebiak and Cane advise waiting for September, when the forecast is generally more reliable, to plan agricultural management strategies.

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